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Antimicrobial activities of essential oils on microorganisms isolated from radiation dermatitis

Antimicrobial activities of essential oils in acute radiation dermatitis

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Abstract
Aim: The aim of this study was to investigate the antimicrobial effect of essential oils obtained from Mediterranean region plants on microorganisms isolated as secondary skin infections in patients with Grade II and III acute radiation dermatitis. Material and Method: The antimicrobial activity of essential oils, Origanum vulgare (O. vulgare), Lavandula intermedia (L. intermedia) and Thymus vulgaris (T. vulgaris) were evaluated by broth microdilution method on microorganisms isolated from 20 patients with Grade II and III radiation dermatitis. Microdilutions had modified according to The Clinical and Laboratory Standards Institute (CLSI) recommendations and lowest concentration which inhibited growth after incubation was identified as Minimal Inhibitory Concentration (MIC). The severity degree of acute radiation dermatitis was graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.03. Results: Nine pathogenic strains were isolated from 20 samples of the patients. The pathogens isolated from skin swabs of the patients with Grade II and III radiation dermatitis were Methicillin-resistant Staphylococcus aureus (MRSA), methicillin-sensitive Staphylococcus aureus (MSSA), methicillin-resistant coagulase-negative Staphylococcus (MRCNS), methicillin-sensitive coagulase-negative Staphylococcus (MSCNS), Klebsiella pneumoniae (K. pneumoniae) and Candida albicans (C. albicans). Minimal Inhibitory Concentration values of O. vulgare, L. intermedia and T. vulgaris for each isolated microorganisms were found. These essential oils have been found effective on microorganisms isolated from secondary infections of radiation-related dermatitis. Discussion: Antimicrobial activity of O. vulgare, L. intermedia and T. vulgaris essential oils on pathogenic microorganisms isolated from radiation dermatitis were determined. Future use of essential oils in the treatment of acute radiation dermatitis should be considered.

Keywords
Radiation Dermatitis; Essential Oils; Antimicrobial Activity

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Introduction

Radiotherapy is one of the mainstay treatment of cancer therapy and about 50% of the patients with cancer receive some type of radiation therapy during their treatment course [1]. Acute radiation dermatitis, which also called acute radiodermatitis is one of the most common side effects of radiotherapy and radiation-related severe skin reactions may necessitate treatment interruption [2]. Usually, acute radiation dermatitis starts within 1-4 weeks after starting radiation treatment (approximately at 20 Gy dose with standard fractionation) and may prolong to 4 weeks after radiotherapy [3]. Both treatment and patient-related some factors are affecting the severity of radiation dermatitis to a certain extent. From radiotherapeutical aspect, location of the tumor, field and fraction size, proximity of the target to the skin, treatment duration, type of energy used and use of any bolus material affect the severity of dermatitis. Patient-related factors can include treatment to sites where two skin surfaces are in contact (e.g. perineum, breast), areas where the skin is thin and smooth (e.g. axilla, face) or skin integrity has already disrupted from surgery, burns or lesions. Patient-related risk factors also can include receiving concurrent radiosensitizing therapies (e.g. antibiotics, chemotherapy, immunotherapy, targeted therapies) or co-morbidities and environmental factors [4,5].

Skin is a protective barrier against infections and the impairment of the skin tissue integrity makes it susceptible to infections. Tissue integrity is impaired in radiation dermatitis and susceptibility to infections increases [6,7]. There are two possible ways of contamination. One of them is the endogenous way which is responsible for the majority of hospital infections. The normally sterile sites are contaminated and then colonized by the flora which is carrying the patient himself, with the favor of a rupture of the barriers. The other one is exogenic way or associated colonization, possibly followed by an infection by external microorganisms coming from other patients or several supporting factors (age, pathology, and certain immunosuppressive treatments) [8].

Essential oils are lipophilic, antioxidant and antimicrobial in their nature and there has been an increased interest in their usage in health care [9,10]. Due to their availability, low cost and negligible side effects these natural medicines have been used for centuries [11]. In this study, antimicrobial activities of *O. vulgare, L. Intermedia,* and *T. vulgaris* essential oils were evaluated on secondary infectious agents isolated from acute radiation dermatitis.

Material and Method

Our study was carried out on 20 patients with Grade II andIII radiation dermatitis who were treated between September and November 2018 in Akdeniz University Radiation Oncology Clinic. The severity degree of radiation-induced dermatitis of the patients was graded according to CTCAE v 4.03. Grade-II changes included moderate to brisk erythema, patchy moist desquamation (mostly confined to the skin folds and creases) and moderate edema. Grade-III was characterized by moist desquamation in areas other than skin folds and creases (minor trauma or abrasion may induce bleeding) [12].

Culture samples were collected with the sterile cotton swabs from patients with Grade II and III radiation dermatitis. The swaps were placed in modified Stuart medium and were sent to the laboratory and inoculated on 5% sheep blood agar, eosin methylene blue agar (EMB) and Sabouraud's dextrose agar. Then, plates were incubated in 35±2 ^{0}C for 18-48 hours. In cultures which have growth, conventional methods or commercial identification kits were used for identification of microorganisms. The antimicrobial activity of essential oils O. vulgare (0,809 gr/ml), L.intermedia (0,752 gr/ml) and T. vulgaris (0,829 gr/ml) were evaluated with serial broth microdilution method. Microdilutions had modified according to The Clinical and Laboratory Standards Institute (CLSI) recommendations and lowest concentration which inhibited growth after incubation was identified as Minimal Inhibitory Concentration (MIC).

Results

Reproduction detected in nine of the totally twenty patient samples. The microorganisms isolated from skin swabs of the patients with Grade II and III radiation dermatitis were *Methicillin-resistant Staphylococcus aureus (MRSA), Methicillin-* sensitive Staphylococcus aureus *(MSSA*), *Methicillin-resistant coagulase-negative Staphylococcus* (*MRCNS), Methicillin-susceptible coagulase-negative Staphylococcus (MSCNS), Klebsiella pneumoniae and Candida albicans*.

Minimal Inhibitory Concentration values for *O. vulgare* were, *MRSA* (MIC: 404,5µg/ml), *MSSA* (MIC: 404,5 µg/ml), *MRCNS* (MIC: 404,5 µg/ml), *MSCNS* (MIC: 202,25 µg/ml), *K. pneumoniae* (MIC: 404,5 µg/ml), *C. albicans* (MIC: 404,5 µg/ml), respectively. Minimal Inhibitory Concentration values for *L. intermedia* were, *MRSA* (MİC: 188 µg/ml), *MSSA* (MIC: 94 µg/ml), *MRCNS* (MIC: 188 µg/ml), *MSCNS* (MIC: 47 µg/ml), *K. pneumoniae* (MIC: 376 µg/ml), *C. albicans* (MIC:188 µg/ml), respectively. Minimal Inhibitory Concentration values for *T .vulgaris* were, *MRSA* (MIC: 414,5 µg/ml), *MSSA* (MIC: 207,25 µg/ml), *MRCNS* (MIC: 207,25 µg/ml), *MSCNS* (MIC: 103,6 µg/ml), *K. pneumoniae* (MIC: 414,5 µg/ml), *C. albicans* (MIC: 207,25 µg/ml), respectively. The *O. vulgare, L. intermedia* and *T. vulgaris* are found effective antimicrobials against bacteria isolated from acute radiation dermatitis. Antimicrobial activity results (MIC, µg/ml) of the selected essential oils on microorganisms isolated from patient samples are shown in the table (Table 1).

Table 1. Selected MIC's (µg/ml) of essential oils against radiation dermatitis pathogens

Gram Positive Bacteria n (%)	O. vulgare (0,809 µg/ml)	L. intermediae (0,752 µg/ml)	T. vulgaris (0,829 µg/ml)
MRSA n: 1 (%11,1)	404,5	188	414,5
MRKNS n: 3 (%33,3)	202,25-404,5	94-188	207,25-414,5
MSSA n: 1 (%11,1)	404,5	188	207,25
MSKNS n: 1 (%11,1)	202,25	47	103,6
Gram Negative Bacteria n (%)			
K. pneumoniae n:1 (%11,1)	404,5	376	414,5
Yeast			
C. albicans n: 2 (%22,2)	404,5	188	207,25

Discussion

Radiation dermatitis continues to be among the most common side effects of radiotherapy and it is a dose-dependent deterministic effect of radiation with predictable dose and timing. In general, the clinical symptoms of severity includes mild erythema, dry desquamation, moist desquamation, and ulcers, respectively [13]. Irradiated tissue with a certain dose becomes susceptible to trauma, infection, and irritation because of destroyed tissue barrier [6,7]. Altoparlak et al. indicated that radiodermatitis leads to an increased risk for secondary infection of the skin with pathogens. Their study suggested that the incidence of superinfections are seemed to be increased in a patient with radiodermatitis and taking control swab samples from the area of radiation dermatitis can be a useful method for early detection and therapeutic interventions of the possible infection [14]. Hill et al. called attention to the role of S. aureus in the pathogenesis of severe radiation dermatitis. They emphasized the importance of adding topical and oral antibiotic therapies to topical steroid applications for radiation dermatitis [2]. Because of their antimicrobial effects, essential oils can be considered as a good alteranatives of synthetic antimicrobial therapies.

Essential oils are extremely effective antimicrobial agents which are secondary metabolites produced by aromatic plants to protect themselves from microorganisms. They also have shown activity against drug-resistant pathogens and can be used as an alternative to synthetic antimicrobial agents [11]. Therefore, their usage in secondary infections related to radiation-induced dermatitis must be considered.

Thabit et al. indicated that antimicrobial resistance is a global threat. Prudent use of currently available antimicrobials, as well as implementing measures to limit the spread of resistance is paramount. Strong infection policies and new therapies are required to reverse this process. Therefore, the importance of interventions to prevent microbial colonization is increasing [15]. In this context, the use of essential oils that may prevent microbial colonization seems possible in patients with secondary infection risk. Vavassis et al. evaluated the silver leaf dressing for treatment of radiation-induced dermatitis in patients receiving radiotherapy to the head and neck region. They concluded that silver dressing does not appear to be superior to their standard treatment in radiation dermatitis [16].

Sakkas et al. found MIC values for *O vulgare* of multiresistance gram negative *Acinetobacter baumanii, Esherichia coli, K. pneumoniae, Pseudomonas aeruginosa* isolates as 0,25-4 %(v/v) [17]. Scandorieiro and colleagues have identified the antimicrobial activity of O. vulgare in multi-drug resistant bacterial strains [18]. In our study, the antimicrobial activity of O. vulgare was determined and the MIC values were, MRSA (MIC: 404.5 Mg / ml), MSSA (MIC: 404.5 edilg / ml), MRCNS (MIC: 404.5 dag / ml), MSCNS (MIC: 202.25 ICg / ml), K. pneumoniae (MIC: 404.5 ICg / ml), C. albicans (MIC: 404.5: g / ml) respectively.

Saccehetti et al. found antimicrobial activity in 11 essential oils including T. vulgaris [9]. Cosentino et al. and Smith-Palmer et al. have also identified antimicrobial activity for T. vulgaris [19,20]. In our study, MIC values of T. Vulgaris was determined as follows: *MRSA* (MIC: 414,5 µg/ml), *MSSA* (MIC: 207,25 µg/ml), *MRCNS* (MIC: 207,25 µg/ml), *MSCNS* (MIC: 103,6 µg/ml), *K. pneumoniae* (MIC: 414,5 µg/ml), *C. albicans* (MIC: 207,25 µg/ml). Cavanagh and Wilkinson investigated biological activities of *L. Intermedia* in their study. They found gram-positive and negative antibacterial, antifungal and wound healing dermatological effects of *L. Intermedia* [21]. Moon and colleagues, determined the antiparasitic activity of *L. intermedia* against *Giardia duodenalis*, *Trichomonas vaginalis* and *Hexaamita inflata* in their study [22]. In our study, MIC values for *L. intermedia* were *MRSA* (MIC: 188 µg/ml), *MSSA* (MIC: 94 µg/ml), *MRCNS* (MIC: 188 µg/ml), *MSCNS* (MIC: 47 µg/ml), *K. pneumoniae* (MIC: 376 µg/ml), *C. albicans* (MIC: 188 µg/ml) respectively.

It is believed that new and large-scale studies are needed for the use of essential oils prophylactically in preventing the development of radiation dermatitis or in the treatment of occured acute radiation dermatitis.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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